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EXAMINER	
KINSEY WHITE, NICOLE ERIN	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
05/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/533,734	ERTL, PETER FRANZ	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-24,28-32 and 36* is/are pending in the application.

4a) Of the above claim(s) *32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-24,28-31 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Withdrawn Rejections

The rejection of claims 1-24, 28-31 and 36 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of applicants' amendments to the claims.

The rejection of claims 1, 2, 4, 5, 12, 13, 17, 18, 21, 22, 28-31 and 36 under 35 U.S.C. 102(b) as being anticipated by Nabel et al. (WO 02/32943) as evidenced by Fynan et al. (Proc. Natl. Acad. Sci. USA, 90: 11478-82, 1993) has been withdrawn in view of applicants' amendments to the claims.

The rejection of claim 3 under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Botarelli et al. (Journal of Immunology, 1991, 147(9):3128-3132) is withdrawn in view of the cancellation of claim 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 5, 12, 13, 17, 18, 21, 22, 28-31 and 36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Botarelli et al. (Journal of Immunology, 1991, 147(9):3128-3132) and Li et al. (Journal of Virology, 1993, 67(1):584-588) and as evidenced by Fynan et al. (Proc. Natl. Acad. Sci. USA, 90: 11478-82, 1993).

The claims are drawn to a pharmaceutical composition comprising a polynucleotide that comprises a sequence encoding an HIV gp120 envelope protein, operably linked to a heterologous promoter, wherein the HIV gp120 envelope protein is lacking a functional secretion signal and is substantially non-glycosylated when expressed in a mammalian target cell, and at least one pharmaceutically acceptable excipient, diluent, and/or carrier.

Nabel et al. discloses various double-stranded DNA vectors comprising sequences that encode an HIV Env that is non-glycosylated (see pages 43, 45 and 46, in particular page 46, lines 13-17) and HIV Env fused to another HIV gene such as Nef (see pages 58-59). The teachings of Nabel et al. include the use of gp120 in the envelope-containing vectors and fusion proteins (see, for example, page 20). The

sequences are under the control of a heterologous promoter (see page 23, lines 6-29), and the env sequences are codon optimized for expression in human cells (page 16, line 30 and pages 58-59). Compositions comprising the vectors can be in aqueous solution (page 25, lines 3-6), mixed with a pharmaceutically acceptable adjuvant (page 27, lines 1-15), enclosed in liposome carriers (i.e., particle carriers) (page 25, lines 9-15), and can be used in a prime-boost regimen (page 27, lines 26-27). In addition, Nabel et al. teaches that the compositions can be administered intramuscularly, intraperitoneally, intradermally, subcutaneously, etc. via intradermal delivery devices such as syringes, needle-less injection devices, or microprojectile bombardment gene guns (page 33, lines 5-13). It is well known in the art that gold beads are used as carriers for DNA vaccinations via gene guns or microprojectile bombardment as evidenced by Fynan et al.

Nabel et al. does not teach gp120 nucleic acid that encodes a non-glycosylated form of gp120 that result from a non-functional secretion signal. Li et al. teaches that non-glycosylated forms of HIV gp120 can be made by deleting the secretion signal of gp120 (see Abstract and introduction). Li et al. states that deletion of the signal sequence of HIV-1 gpl20, which represents 30 amino acids at the N terminus, results in the synthesis of large quantities of a nonglycosylated and nonsecreted form (see page 584, right column).

Botarelli et al. teaches that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes (see abstract). The non-glycosylated form of HIV gp120 of Botarelli et al. was produced by removing the

signal sequence. Botarelli et al. states that "[t]he lack of signal sequence prevents passage through the secretory pathway and addition of carbohydrates."

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use HIV env sequences lacking a secretory signal sequence to produced non-glycosylated HIV Env. One would have been motivated to do so, given the fact that deletion of the secretion signal is a routinely used method to produce non-glycosylated proteins. One also would have been motivated given the suggestion by Botarelli et al. that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes. There would have been a reasonable expectation of success, given the fact that it is well known that the removal of the secretory signal sequence bypasses the secretory pathway and the addition of carbohydrates, and that others have successfully produced non-glycosylated proteins by removing the secretory signal sequence (see Botarelli et al. and Li et al.). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In the reply filed on February 11, 2008, applicants argue that the proteins of Nabel et al. did not substantially enhance humoral or CTL immunity. Applicants further argue that Botarelli cannot be viewed as providing a motivation to vaccinate with a non-glycosylated form of Env nor can Botarelli be viewed as providing a reasonable expectation that such a vaccine would be successful.

However, the claims are drawn to, *inter alia*, a pharmaceutical composition comprising a polynucleotide that comprises a sequence encoding an HIV gp120 envelope protein, operably linked to a heterologous promoter, wherein the HIV gp120 envelope protein is lacking a functional secretion signal and is substantially non-glycosylated when expressed in a mammalian target cell, and at least one pharmaceutically acceptable excipient, diluent, and/or carrier, and the combination of references, as outlined above, teaches each limitation of the claimed invention.

Contrary to applicants' assertion, the constructs of Nabel et al. did produce immune responses. Nabel et al. states that mice immunized with codon-altered Env vectors, including COOH-terminal deletion mutations or glycosylation mutants, elicited strong CTL responses directed to cell lines pulsed with HIV Env peptides (see page 45). Thus, one of ordinary skill in the art would be motivated to use non-glycosylated forms of gp120 as a vaccine.

Claims 15 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Catchpole et al. (WO 02/36792).

Claims 15 and 16 are drawn to the polynucleotides of the invention linked to the HCMV IE gene promoter and also the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). Nabel et al. does disclose the use of the CMV promoter (page 31, lines 31-32), but not the use

of the HCMV IE gene promoter or the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene.

Catchpole et al. teaches that the use of the HCMV IE gene promoter to drive gene expression is known (page 1, lines 19-33). Catchpole et al. further states that the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene will result in an enhanced level of expression from the HCMV IE promoter (page 2, line 25 to page 4, line 2). Catchpole et al. also teaches that such promoter sequences are good for the expression of HIV antigens (page 5, line 32 to page 7, line 4).

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use the HCMV IE promoter and 5' sequences from HCMV IE in order to express HIV antigens/genes. One would have been motivated to do so, given the suggestion by Nabel et al. to use the CMV promoter generally to express HIV antigens and the suggestion by Catchpole et al. to use the HCMV IE promoter specifically to drive expression of recombinant proteins and to use the 5' untranslated sequences for enhanced expression of antigens. There would have been a reasonable expectation of success, given the fact that it is well known that the CMV promoter is a strong promoter and that the CMV promoter is commonly used to express heterologous proteins/antigens (see Catchpole et al., page 1, lines 19-33), including HIV antigens. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Farina et al. and Roy et al.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). Nabel et al. does disclose the use of adenovirus as a vector (page 25, lines 16-35), but not a replication-defective adenovirus or Pan 9, 5, 6, or 7.

Farina et al. teaches the use of replication-defective adenovirus C68 to express genes. C68 is another name for Pan 9 as evidenced by Roy et al.

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use the C68 (Pan 9) replication-defective adenovirus of Farina et al. One would have been motivated to do so, given the suggestion by Farina et al. that C68 functions as an excellent vaccine for HIV (see Farina et al. page 11612, last paragraph of the discussion) and that humans rarely have neutralizing antibodies to these viruses. There would have been a reasonable expectation of success, given the fact that it is well known to use replication-defective adenoviruses as vaccine vehicles. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 4 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jiang et al. (Chinese Journal of Microbiology and Immunology, 2002, 22(5):482-484)(Abstract only) in view of Botarelli et al. (Journal of Immunology, 1991, 147(9):3128-3132).

Jiang et al. teaches an HIV gp120-gag fusion protein antigen expressed in yeast from the yeast expression vector pHILS1.

Botarelli et al. teaches that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes (see abstract). The non-glycosylated form of HIV gp120 of Botarelli et al. was produced by removing the signal sequence. Botarelli et al. states that "[t]he lack of signal sequence prevents passage through the secretory pathway and addition of carbohydrates."

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Jiang et al. to use HIV gp120 sequences lacking glycosylation. This can be achieved by removing the secretory signal sequence as taught by Botarelli et al. or by mutating glycosylation signals. One would have been motivated to do so, given the suggestion by Botarelli et al. that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes. There would have been a reasonable expectation of success given the fact that it is well known in the art that mutating glycosylation signals and/or removing the secretory signal sequence to bypasses the secretory pathway both result in non-glycosylated forms of the peptide. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-24, 28-31 and 36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20, 24-27 and 32 of copending Application No. 11/734,464. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a recombinant polynucleotide molecule comprising HIV envelope sequences fused to at least one HIV nonstructural protein or capsid protein in a vector with a heterologous promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 4, 6, 7, 10-14 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9, 10, 13-16 and 18-21 of U.S. Patent No. 10/490,011. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a recombinant polynucleotide molecule comprising gp120 sequences, a heterologous promoter and an other HIV proteins such as Nef and/or Tat in a vector with an enhanced HCMV IE1 promoter. For example, the gp120-RT-Nef-Gag peptide of instant claim 7 would also read on the claims of co-pending application 10/490,011.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nicole Kinsey White, PhD/
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648